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IAP14 Rec'd PCT/PTO 8 AUG 2006

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)**

International application No.
PCT/EP2005/050800

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claims 15-19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

2. Reference is made to the following documents:

**D1**: WO 02/069945 A (BOEHRINGER INGELHEIM PHARMA ; PIEPER MICHAEL PAUL (DE); PAIRET MICHEL) 12 September 2002;
**D2**: US 2004/002548 A1 (BOZUNG KARL-HEINZ ET AL) 1 January 2004;
**D3**: EP-A-1 369 129 (ONO PHARMACEUTICAL CO) 10 December 2003;
**D4**: DE 100 61 137 A (BYK GULDEN LOMBERG CHEM FAB) 20 June 2002.

If not indicated otherwise, the relevant passages are those mentioned in the International Search Report.

3. The present application according to **claim 1** relates to a pharmaceutical formulation comprising a pharmaceutically acceptable salt of glycopyrronium, a solvates or physiologically functional derivative thereof in combination with an active pharmaceutical ingredient being a compound selected from the group consisting of roflumilast, pharmaceutically acceptable salts thereof, solvates or physiologically functional derivative thereof and a pharmacologically acceptable carrier and/or more excipients. **Claim 15** is direct to a method for the prophylaxis or treatment of a clinical condition in a mammal which comprises the administration of the combination according to claim 1. In claim 16 the clinical condition is specified in a given list.

4. The present application meets the requirements of the PCT with respect to novelty (Art. 33(2)). None of the documents of the prior art discloses the specific therapeutic combination of roflumilast and glycopyrrolate, as in the present application. Accordingly, the pharmaceutical compositions of claims 1-14, 20, and the method according to claims 15-19 are novel.

5. However, no inventive step can be recognised in the subject-matter of present claims 1-20 (Art. 33(3) PCT) for the following reasons.

**D1**, which is regarded as the closest prior art, discloses pharmaceutical compositions useful for the treatment of respiratory tract disorders, comprising a PDE4 inhibitor in combination with an anticholinergic. Roflumilast is disclosed as a preferred PDE4 inhibitor. The present application differs from **D1** in that roflumilast is combined specifically with the anticholinergic agent glycopyrrolate. The applicant asserts that a synergistic effect arises from this combination. However, as far as this effect is not properly substantiated by technical data, said alleged effect can not be taken into account for the assessment of inventive step. Thus, the problem to be solved by the present application can only be regarded as the provision of alternative combinations of roflumilast with anticholinergic agent useful for the treatment of respiratory disorders.

The solution provided by the present application is rendered obvious by **D2**. Said document discloses the compound glycopyrronium as an anticholinergic agent useful in the treatment of respiratory disorders such as asthma or COPD. In the light of this document the skilled person would regard it obvious to consider the combination of roflumilast with glycopyrrolate as an alternative to those disclosed in **D1**.

It appears that in order to recognised an inventive step, the applicant should provide any kind of evidence supporting the alleged synergistic effect.

6.1. Claims 1-14 and 20 meet the criterion set forth in Article 33(4) PCT because their subject-matter is susceptible of industrial application.

6.2. For the assessment of the present claims 15-19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The

patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.